

CLAIMS

What is claimed is:

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- 66T30" 6634E60
1. A method for identifying and isolating non-redundant nucleic acid fragments, comprising:
 - (a) providing a random sample of nucleic acid fragments;
 - (b) immobilizing the random sample of nucleic acid fragments on a microarray;
 - (c) hybridizing one or more labeled probes corresponding to previously arrayed or sequenced fragments;
 - (d) detecting fragments hybridized to the labeled probes and identifying at least one fragment not hybridized or weakly hybridized to the labeled probes; and
 - (e) sequencing a fragment identified in step (e) that was not hybridized or was weakly hybridized to the labeled probes.
 2. The method of claim 1, wherein the nucleic acid fragments comprise DNA.
 3. The method of claim 2, wherein the DNA is cDNA.
 4. The method of claim 2, wherein the DNA is genomic DNA.
 5. The method of claim 3, wherein the DNA is a clone from a library.
 6. The method of claim 4, wherein the DNA is a clone from a library.
 7. The method of claim 1, wherein the nucleic acid fragments comprise RNA.
 8. The method of claim 1, wherein the nucleic acid fragments are amplified.
 9. The method of claim 8, wherein the amplification is PCR amplification.
 10. The method of claim 1, wherein the label is selected from the group consisting of a fluorescent label, a luminescent label, and a radioactive label.
- Sub A2

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11. A method for enhancing the rate of discovery of expressed mRNA/cDNA sequences and facilitating construction of a "UniGene" set comprising:
- (a) amplifying a random sample of nucleic acid fragments;
 - (b) immobilizing the random nucleic acids on a solid surface in a microarray format;
 - (c) hybridizing labeled probes from a DNA source to the immobilized, microarrayed DNA fragments;
 - (d) detecting DNA fragments hybridized to a labeled probe and identifying at least one fragment that does not hybridize or hybridizes weakly;
 - (e) determining the identity of the DNA fragment by DNA sequencing, hybridization or other analytic approaches; and
 - (f) reiterating steps (b) or (c) through (e) with previously identified sequences in the probe set in order to identify additional sequences and increase the UniGene set.
12. A method for enhancing the rate of discovery of genomic sequences and facilitating isolation of a DNA fragments corresponding to a whole genome or subregions of interest, the method comprising:
- (a) amplifying a random sample of genomic nucleic acid fragments;
 - (b) immobilizing the random nucleic acids on a solid surface in a microarray format;
 - (c) hybridizing labeled probes from a DNA source to the immobilized, microarrayed DNA fragments;
 - (d) detecting DNA fragments which hybridize to a labeled probe;
 - (e) determining the identity of the DNA fragment by DNA sequencing, hybridization or other analytic approaches; and
 - (f) reiterating steps (b) or (c) through (e) with previously identified sequences in the probe set in order to identify additional sequences and increase the UniGene set.
- B 13. The method of claim ²⁶11, wherein the labeled probes are pooled labeled probes or single labeled probes. ₁
- B 14. The method of claim ²⁶11, wherein the labeled probes are cDNA/mRNA or genomic sequences. ₁

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15. A method for enrichment and/or isolation of DNA sequences that are unique to a population compared to another population, comprising:
- (a) amplifying and providing a random sample of nucleic acid fragments;
 - (b) immobilizing the random nucleic acids on a solid surface in a microarray format;
 - (c) hybridizing labeled probes from a first source and labeled probes from a second source to the immobilized, microarrayed DNA fragments;
 - (d) detecting DNA fragments which hybridize to a labeled probe from the first source or the second source; and
 - (e) determining the identity of the DNA fragment by DNA sequencing, hybridization or other analytic approaches.

16. The method of claim 15, wherein the random sample of nucleic acid fragments is amplified by PCR or nucleic acid isolation procedures.

17. The method of claim 15, wherein the labeled probes are cDNA/mRNA or genomic sequences.

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18. A method for increasing discovery of related DNA sequences comprising:

- (a) amplifying a random sample of nucleic acid fragments;
- (b) immobilizing the random nucleic acids on a solid surface in a microarray format;
- (c) hybridizing labeled probes to the immobilized, microarrayed DNA fragments, particularly at decreased hybridization stringencies;
- (d) detecting DNA fragments which hybridize weakly to a labeled probe;
- (e) determining the identity of the DNA fragment by DNA sequencing, hybridization or other analytic approaches; and
- (f) comparing DNA sequences obtained to other available DNA sequences to detect sequences which show homology but are not identical to other known sequences.

19. The method of claim 18, wherein the labeled probes are cDNA/mRNA or genomic sequences.

20. The method of claim 18, wherein the labeled probes are pooled labeled probes or single labeled probes.

21. A method for enhancing the rate of removal of undesired sequences comprising:

- (a) amplifying a random sample of nucleic acid fragments;
- (b) immobilizing the random nucleic acids on a solid surface in a microarray format;
- (c) hybridizing labeled probes, which are sequences targeted for removal, to the immobilized, microarrayed DNA fragments;
- (d) detecting DNA fragments hybridized to a labeled probe and identifying at least one fragment that does not hybridize or hybridizes weakly;
- (e) determining the identity of the DNA fragment by DNA sequencing, hybridization or other analytic approaches; and
- (f) reiterating steps (a) or (b) or (c) through (e) with previously identified sequences in the probe set, as deemed necessary, in order to eliminate unwanted sequences from the population of fragments.

22. A method for identifying changes in copy number of DNA sequences between different sources of nucleic acids, comprising:

- (a) amplifying a random sample of nucleic acid fragments from a given source;
- (b) immobilizing the random nucleic acids on a solid surface in a microarray format;
- (c) hybridizing labeled probes from another source to the immobilized, microarrayed DNA fragments;
- (d) detecting DNA fragments which show absent, significantly lesser or significantly greater hybridization to a labeled probe relative to fragments from another source; and
- (e) determining the identity of the DNA fragment(s) by DNA sequencing, hybridization or other analytic approaches.

23. The method of claim 22, wherein the copy number of DNA sequences is under-represented.

24. The method of claim 22, wherein the copy number of DNA sequences is over-represented.

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B¹

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continued